CLINICAL AND ETIOLOGICAL CORRELATIONS IN CEREBRAL PALSY

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ABSTRACT

Cerebral palsy (CP) is a group of persistent (but not necessarily unchanged), movement, posture, muscle tone, and motor skills disorders, with early onset, due to non-progressive impairments, occurring on an immature brain or a brain under development (prenatal, perinatal, postnatal during the first 3-4 years of life). It is associated to a variable extent with: cognitive disorders, epilepsy, sensory deficits, behaviour disorders.

The aim of this study. The study of the correlations between the clinical forms/subtypes of CP and aetiology.

Material and method. It is a retrospective trial aimed only at patients with the diagnosis of cerebral palsy admitted at Paediatric Neurology Clinic of the Clinical Hospital "Alexandru Obregia" in 2010.

Results and discussions. Patients with cerebral palsy corresponding with the criteria for inclusion: 379 CP was due to prenatal aetiology in 32.45% cases, perinatal aetiology in 60.15% case, postnatal aetiology in 10.8 % cases. Prenatal aetiology was represented mostly by malformations 43.1%. Compared with perinatal or postnatal aetiologies, ataxic forms were more frequently of prenatal cause. The unilateral spastic form was correlated significantly from a statistical point of view with prenatal aetiology – malformations (p0.003) and the dyskinetic form with unknown prenatal aetiology. Mental retardation was present in 86.4% of the cases with assumed prenatal aetiology and was severe in 38.2% of the cases. The perinatal aetiology was represented by PVL 32% haemorrhage 21.1%, hypoxia 18.4%, stroke 14%, the aetiology being unknown in 7% of the cases. The distribution was comparable to that of other causes with a higher frequency of dyskinetic forms. The correlations between the perinatal aetiology and the clinical forms were (p0.000): LPV with spastic diplegia and tetraplegia, perinatal stroke with spastic hemiplegia, perinatal hypoxia with ataxic and dyskinetic forms, peri/intraventricular haemorrhage with spastic tripegia. Perinatal aetiology was correlated significantly with retardation as follows: perinatal stroke with the absence of mental delay, and hypoxia with severe and profound retardation (p0.001) Postnatal aetiology had: infections 36.6%, stroke 17%, stabilized hydrocephaly 17%, cardio-respiratory arrest 9.8%, trauma 7.3%. The number of cases was too small for significant correlations.

Conclusions. Aetiology and the time of the occurrence of the lesion are important in cerebral palsy.

Key words: cerebral palsy, clinical type, aetiology

INTRODUCTION

Cerebral palsy (CP) is a group of persistent (but not necessarily unchanged), movement, posture, muscle tone and motor skills disorders non-progressive, with early onset, due to non-progressive impairments, occurring on an immature brain or a brain under development (prenatal, perinatal, postnatal during the first 3-4 years of life). (1) It is associated to a variable extent with: cognitive disorders, epilepsy, sensory deficits, behaviour disorders. The aetiology of cerebral palsy is sometimes difficult to identify, and neuroimaging plays an important role in this respect.

THE AIM OF THE STUDY

Establishment of correlations between the clinical forms/subtypes of CP, comorbidities, the severity of functional motor impairment (GMFCS) and aetiology.

MATERIAL AND METHOD

It is a retrospective trial aimed only at patients with the diagnosis of cerebral palsy according to the ICD 10 (International Classification of Diseases – tenth revision). (2) admitted at Paediatric Neurology Clinic of the Clinical Hospital "Alexandru Obregia", between 01.01.2010 and 31.12.2011.

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All patients with the diagnosis of cerebral palsy were reassessed retrospectively based on data recorded in their medical observation sheet based on the previous records, development, clinical examination, laboratory and paraclinical examinations.

Inclusion criteria: patients with the diagnosis of cerebral palsy and who underwent cerebral imaging (cerebral computed tomography – CT or magnetic resonance imaging – MRI).

Exclusion criteria: static movement disorders with an onset after the age of 3, more or less progressive movement disorders or psychomotor retardation due to progressive causes; the presence of sensory deficits occurred in the development, ataxia, muscle atrophy, involuntary movements; medullary lesions; movement disorders caused by muscles or peripheral motor neuron disease, hypotonic syndromes, patients with a family history of "cerebral palsy", the presence of unexplainable acute episodes of vomiting, diarrheea, consciousness disorders, abnormal movements, mental or endocrine disorders (growth hormone deficit, adrenal insufficiency, diabetes), patients aged under 1.

From a clinical point of view cerebral palsy was classified according to the classification from 2002 of SCPE (European Cooperation on Surveillance of Cerebral Palsies in Europe) in (3): spastic; ataxic; dyskinetic; dystonic; choreoathetosic, and refers to a muscle tone, motion and dominant posture disorder.

ETIOLOGICAL DIAGNOSIS

I defined **prenatal/antenatal causes** as any disruptive factor acting from the time of the conception until the time of the onset of labour.

I considered **prenatal** causes the following:

- cerebral malformations revealed imagistic
- intrauterine infections (serological diagnostic)
- prenatal stroke when there was imaging suggestive of lesion in the vascular area prenatal, porencephalic lesion present at birth
- microcephaly present since birth,
- encephalomalacia demonstrated at birth
- antenatal hydrocephalia, demonstrated by ultrasound
- hydranencephaly
- dysmorphia or phenotype particularly suggestive of genetic anomaly
- absence of any postnatal or perinatal factor

Prenatal periventricular leukomalacia (LPV) – imagery suggestive of LPV, in the absence of perinatal impairment, or premature birth.

Neonatal clinical signs suggesting prenatal damage (Amiel-Tison, 1997) (4): fingers clenched in a fist with the thumb tight and retracted, ogival palate, prominent squamous suture.

I defined **perinatal** as the factor which acted from the onset of labour, during birth and/or during the first 7 days after birth.

For acute **hypoxia** (asphyxia) at birth, the criteria were:

- documented signs of moderate or severe neonatal hypoxic-ischemic according to the Sarnat and Sarnat with early onset (24 h), in new-borns with gestational age above than 34 weeks (5).
- exclusion of other neonatal encephalopathy aetiologies (trauma, infection, clotting disorders or genetic diseases)
- and at least 3 of the following: evidence of metabolic acidosis in the foetal umbilical arterial blood harvested at birth (pH below 7, and base deficit greater than 12 mmol/l), Apgar score < 6 to ≥ 5 minutes, abnormal coloration of the amniotic fluid, prolonged and late foetal bradycardia, the need for resuscitation at birth, an hypoxic signal event immediately before or during labour (uterine rupture, abruptio placentae, cord prolapse, amniotic embolism, maternal-foetal haemorrhage, maternal cardiac arrest), early imaging signs of non-focal acute cerebral anomalies (for example an acute cerebral oedema with or without haemorrhage), multi-organ damage within 72 h of birth, convulsions in the first 72 h since birth.

For **periventricular/intraventricular haemorrhage** the diagnosis was put on the transfontanelar ultrasound or cerebral CT carried out during the first week after childbirth.

For **perinatal stroke** – the diagnosis was put on imaging aspects of lesion in vascular territory present after childbirth and without clinical signs suggesting a postnatal stroke.

The diagnosis of **trauma** was put on a suggestive anamnesis and related imaging lesions.

LPV was diagnosed by late characteristic postnatal MRI or CT (more often after 1-2 years)

Infections were diagnosed only if they were documented in the first 7 days after birth (diagnosis of meningitis or neonatal sepsis in the patient's medical records)

Hyperbilirubinemia was considered significant in case it determined a more pronounced jaundice which require prolonged, repeated phototherapy, along with the anamnestic data regarding Rh or

group incompatibility, the documents in the maternity certifying hyperbilirubinemia, clinical signs of acute bilirubinemic encephalopathy, the need for exsanguinotransfusion in maternity.

I considered **postnatal** factors, those factors that occurred after the 7th day postnatal, diagnosis supported by anamnesis data suggestive of an acute postnatal event occurred after a period of normality of over 7 days postnatal and paraclinical and imaging associated data to support the etiologic diagnosis.

Where the diagnosis was not certain the aetiology was considered unknown.

Statistical analysis was used to compare the differences between groups and variables and consisted of applying the student's **t-test** – for correlations of 2 variables and chi square for more than 2 variables. The value $p < 0,05$ is of statistical importance.

RESULTS AND DISCUSSIONS

Patients with cerebral palsy corresponding with the criteria for inclusion: **379 of 495** identified with this diagnosis in the range of time mentioned it's composed from: girls 159 (42%), boys 220 (58%), with a M/F ratio 1.38:1.199 children (52.5%) are coming from urban area and 180 children (47.5%) are from rural area. The children were aged between1 and 17: average age 5.94 years (5 years and 11 months).

The estimated time of the occurrence of the lesion was classified as:

- Prenatal aetiology: 32.45% cases (123 cases)
- Perinatal aetiology: 60.15% cases (228 cases)
- Postnatal aetiology: 10.8 % cases (41cases)

The data are superposable with the existing data in the literature – respectively 28% prenatal, 39% perinatal, 5% postnatal according to Himmelmann 2005 (6), or 26% prenatal, 54% perinatal, 3% postnatal, according to Yin 2000 (7). The number of patients with CP of postnatal aetiology was comparably smaller than the rest; therefore a statistically significant analysis for some aetiologies would require a long time and a larger number of patients.

CORRELATIONS OF THE IDENTIFIED AETIOLOGIES

Prenatal aetiology was represented mostly by malformations 43.1% (dysplasia, schizencephaly, hemimegalencephaly, polymicrogyria 53 cases), PVL 17.1%, (21 cases) and prenatal infections 14 cases (11.4%). Prenatal aetiology was unknown 12.2% of the cases (15 cases).

Correlations with the clinical form: Prenatal aetiologies resulted in 46.3% bilateral spastic forms 25.5% unilateral spastic, 16.3% ataxic, 12.2% dyskinetic in my study. (Fig. 1)

Compared with perinatal or postnatal aetiologies, ataxic forms were more frequently of prenatal cause. The observation is consistent with the data in the literature (8).

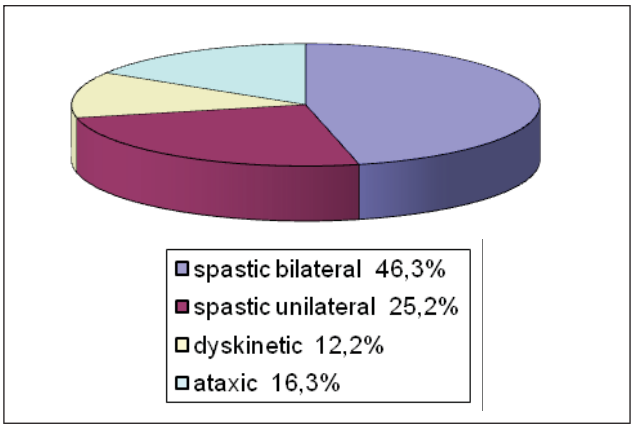

FIGURE 1. *Distribution of clinical type of CP of prenatal aetiology*

64% of prenatal unilateral spastic CP cases were due to malformations, as well as 60% of the prenatal ataxic forms. Most studies give smaller percentages: 20-40%, although it is assumed that prenatal aetiology is more frequent. (8)The unilateral spastic form was correlated significantly from a statistical point of view with prenatal aetiology – malformations (p0.003) and the dyskinetic form with unknown prenatal aetiology (Table 1).

CORRELATIONS WITH MENTAL RETARDATION

Children who had prenatal PC had normal intellect in only 14.6% of the cases (18 cases). Mental retardation was present in 86.4% of the cases with assumed prenatal aetiology and was severe in 38.2% of the cases (47 cases), moderate 21.1% (26 cases), profound (16 cases) 13%, mild 13% (16 cases). Prenatal aetiology multicystic encephalomalacia was correlated significantly from a statistical point of view with profound mental retardation compared to severe retardation (p0.005) (but the number of cases was too small). Prenatal infections had severe retardation or profound retardation without being significant statistically. The intellect was normal in most prenatal stroke. The observations are consistent with the data in the literature (8).

TABLE 1. *Corelations prenatal aetiology-clinical form of CP*

	Clinical form of CP													
	Spastic bilateral diplegia		Spastic bilateral tripegia		Spastic bilateral tetraplegia		Spastic hemiplegia		Dyskinetic		Ataxic		Total	
	n	N%	n	N%	n	N%	n	N%	n	N%	n	N%	n	N%
Malformations	8	36.4%	1	50.0%	8	24.2%	20	64.5%	4	26.7%	12	60.0%	53	43.1%
Infections	1	4.5%	0	.0%	9	27.3%	2	6.5%	2	13.3%	0	.0%	14	11.4%
stroke	0	.0%	0	.0%	0	.0%	4	12.9%	0	.0%	1	5.0%	5	4.1%
PVL	7	31.8%	1	50.0%	6	18.2%	2	6.5%	2	13.3%	3	15.0%	21	17.1%
Genetic	2	9.1%	0	.0%	1	3.0%	0	.0%	0	.0%	2	10.0%	5	4.1%
Cystic encephalomalacia	1	4.5%	0	.0%	5	15.2%	0	.0%	1	6.7%	0	.0%	7	5.7%
Hidranencephaly	0	.0%	0	.0%	2	6.1%	0	.0%	0	.0%	0	.0%	2	1.6%
Hidrocephalia	0	.0%	0	.0%	0	.0%	1	3.2%	0	.0%	0	.0%	1	.8%
Unknown	3	13.6%	0	.0%	2	6.1%	2	6.5%	6	40.0%	2	10.0%	15	12.2%
Total	22	100.0%	2	100.0%	33	100.0%	31	100.0%	15	100.0%	20	100.0%	123	100.0%

Pearson Chi-Square Tests		
		CP type
Prenatal aetiology	Chi-square	68.796
	df	40
	Sig.	.003*,a,b

CORRELATIONS WITH OTHER DISORDERS

An unknown aetiology was correlated significantly from a statistical point of view (which often had normal imaging) with the absence of epilepsy (p0.025). The type of perinatal aetiology was correlated with the **type of epilepsy** (p0.379), but the percentage of patients with generalized epilepsy was higher as compared to the focal type (the number of cases is too small to be of statistical significance).

Another frequent disorder associated with most prenatal causes (except for genetic causes) was the visual/ocular type. Over 40% of the prenatal causes resulted in CP with associated ocular/visual disorders. Prenatal aetiology most often associated with the disorders or comorbidities from prenatal CP was represented by malformations, without being significant statistically. Prenatal infection was associated significantly from a statistical point of view with microencephaly (p0.048).

2. The perinatal aetiology was represented by PVL 32% (73 cases), haemorrhage 21.1% (48 cases), hypoxia 18.4% (42cases), stroke 14% (32 cases), the aetiology being unknown in 7% (16) of the cases. (Fig. 2)

Correlations with clinical forms of CP (Fig 3.) caused by an assumed perinatal cause: the following were identified: spastic diplegia 35% (80 cases), triplegia 3.9% (9 cases), tetraplegia 12.3% (28 cases) (total bilateral spastic forms 51.3%), spastic hemiplegia 23.7% (54 cases), dyskinetic form

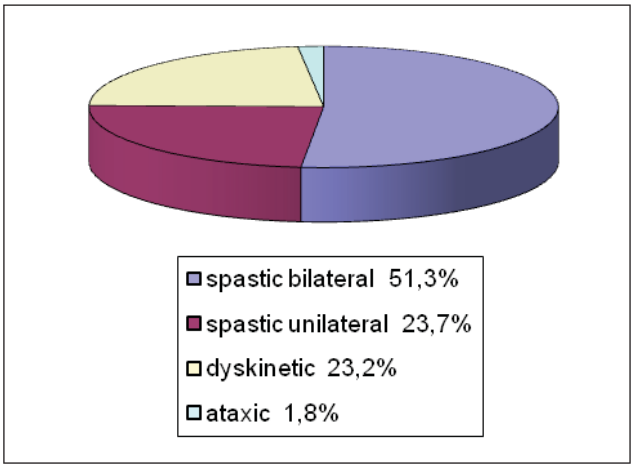

FIGURE 2. *Distribution of clinical CP type of perinatal aetiology*

23.2% and ataxic 1.8% (4 cases). The distribution was comparable to that of other causes with a higher frequency of dyskinetic forms. Almost 97% of perinatal stroke resulted in spastic hemiplegia and only 3% in tripegia. 56% of perinatal PVL and 46% of peri/intraventricular haemorrhage resulted in spastic diplegia, and 47.6% of the cases of perinatal hypoxia had dyskinetic forms. The correlations between the perinatal aetiology and the clinical forms were (p0.000): LPV with spastic diplegia and tetraplegia, perinatal stroke with spastic hemiplegia, perinatal hypoxia with ataxic and dyskinetic forms, peri/intraventricular haemorrhage with spastic tripegia, which is consistent with the data in the literature.(8)

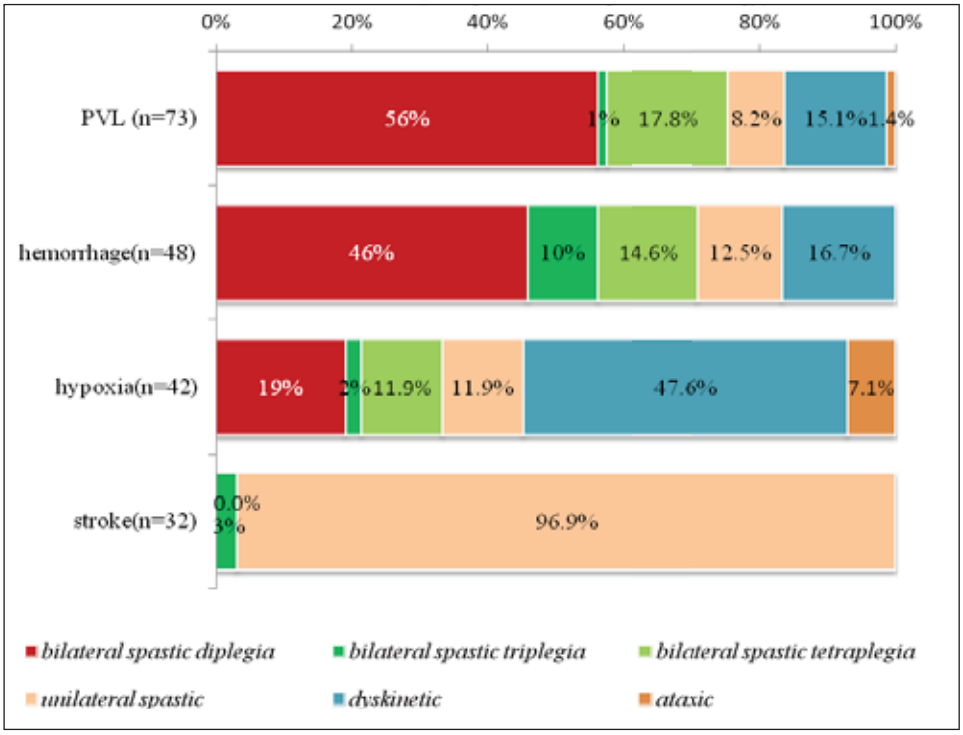

FIGURE 3. *Distribution of CP type according to the specific perinatal aetiology*

Correlations with epilepsy: Epilepsy was present in 46.5% of the perinatal cases and there were no significant correlations with the types of perinatal aetiologies. There were significantly (p0.03) more generalized epilepsies in patients with CP of hypoxic perinatal aetiology, and more focal epilepsies in the CP group of perinatal stroke (although here the number of patients was smaller). The finding is consistent with the type of lesion.

Correlations with mental retardation: Mental retardation was absent in 23.2%, there was mild mental retardation in 22.4% of the cases, moderate in 18% of the cases, severe in 23.6% of the cases, profound in 10% of the cases. Perinatal aetiology was correlated significantly with retardation as follows: perinatal stroke with the absence of mental delay, and hypoxia with severe and profound retardation (p0.001). The data is consistent with the data in the literature.

Associations of statistical significance between perinatal aetiology and other comorbidities (p0.023). Haemorrhage and LPV were associated with ocular/visual disorders, stroke and unspecified aetiology were associated with absence of comorbidities. Hypoxia was associated with microcephaly (0,023).

3. Postnatal aetiology had infections 36.6% (15 cases), stroke (7 cases) 17%, stabilized hydrocephaly 17% (7 cases), cardio-respiratory arrest 9.8% (4 cases), trauma 7.3% (3cases), epilepsy 4.9% (2cases). (Fig. 4)

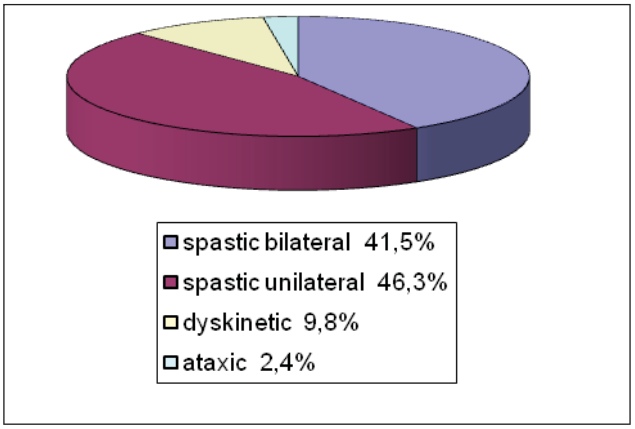

FIGURE 4. *Distribution of clinical CP type of postnatal aetiology*

Correlation with clinical forms: The clinical forms of postnatal CP were: bilateral spastic 41.5%, unilateral spastic 46.3%, dyskinetic 9.8%, ataxic 2.4%. The distribution of clinical forms in CP caused postnatally indicated a higher frequency of the unilateral spastic forms compared to prenatal or perinatal causes. 60% of the children with postnatal infections had spastic tetraplegia, 66.7% had epilepsy and 55% severe and profound retardation. Unilateral spastic forms were presented after postnatal stroke, trauma, operated abscess, stabilized hydrocephaly. Spastic diplegia occurred after cardio-respiratory arrest and stabilized hydrancephaly (here an ataxic form and a dyskinetic form were found). The number of cases was too small for significant correlations. The only significant correla-

tion was between postnatal cardio-respiratory arrest and spastic bilateral diplegic CP.

Correlations with comorbidities: The comorbidities present in CP acquired postnatal were not correlated significantly from a statistical point of view with the types of postnatal aetiologies, the number of cases being small. There was a higher percentage of ocular/visual disorders associated with the following aetiologies: epilepsy, hydrocephaly.

CONCLUSIONS

Aetiology and the time of the occurrence of the lesion are important in cerebral palsy. Finding the aetiology and pathogeny is the first step in finding treatment and prophylaxis.

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